REMARKS / ARGUMENTS

I. Amendments to the claims

Claims 44-60, 63-85 remain in this application. Claims 44-60, 79 and 83 are under examination. Claims 88-93 are added. The Examiner is requested to enter and examine claims 88-93.

Claims 44, 45, 47, 50-59, 79 and 83 are amended to more clearly and particularly claim the invention, as described in more detail below. Because these amendments do not introduce new matter, entry thereof by the Examiner is requested.

Claim 44 is amended to recite --An isolated nucleic acid--. Basis for the amendment is found at page 10 line 28 to page 11 line 7.

Claims 44, 51, 52 and 59 are amended to delete reference to "immunogenic fragment" and "at least 38 consecutive nucleotides".

Claims 51-57 and 83 are amended to recite --vaccine vector-- rather than "vaccine".

Claim 79 is amended to delete part (e).

All amendments not addressed above are for further clarity.

Dependent claims 88-93 are added. Claims 88 and 89 specify that the --expression control sequences comprise a promoter for expression of the nucleic acid in a mammalian cell--. Claims 90 and 91 specify that the promoter is viral. Claims 92 and 93 specify the CMV promoter. Basis for these claims is found at least at page 23, lines 6-8, which state that the promoter is chosen such that it is functional in selected host systems. Page 25, lines 26-28l oage 26, lines 29-34; and page 28, line 34 to page 29, lines 12 state that the promoter is suitable for expression in a mammalian cell. Page 29, lines 13-23 and page 23 lines 29 gives examples of such promoters as the T7, CMV and RSV and desmin promoters. Examples 2 and 3-

describe use of the CMV promoter to drive expression of the nucleic acids of the invention in mice.

Because these amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested. Applicants retain the right to present claims drawn to the cancelled subject matter in a divisional application(s).

II. Rejection of the Claims Under 35 U.S.C. §101

The Examiner rejects claims 44 and 47-50 under 35 U.S.C. §101 as being drawn to non-statutory subject matter. Applicants traverse.

Claim 44 as amended recite --An isolated nucleic acid--. Claims 47-50 already recites --An isolated nucleic acid--. This ground for rejection is now moot, and withdrawal thereof is respectfully requested.

III. Rejection of the Claims Under 35 U.S.C. §112 first paragraph

The Examiner rejects 44, 46-57, 59, 60, 83, 86 and 87 under 35 U.S.C. §112 first paragraph (written description and enablement) with respect to fragments. Applicants traverse.

The claims have been amended to remove references to fragments. As amended, the claims do meet the requirements of 35 U.S.C. §112 first paragraph. Accordingly, withdrawal of this ground for rejection is respectfully requested.

IV. Rejection of the Claims Under 35 U.S.C. § 102(a) -- Kalman Accession No. AE001619 ('Kalman')

The Examiner rejects claims 44-62, 79, 86 and 87 under 35 U.S.C. §102(a), in view of Kalman. The Examiner states that the reference date is 12/1/98. Applicants traverse this ground for rejection.

(a) Kalman was first seen on March 8, 1999, not December 1, 1998

Applicants submit a printout from the NCBI sequence database showing the Revision history of sequence Accession No. AE001619. The revision history of a

sequence on the NCBI database is found at http://www.ncbi.nlm.nih.gov/entrez/sutils/girevhist.cgi.

According to the NCBI, "Accession AE001619 was first seen at NCBI on Mar 8 1999 5:32". The Examiner is therefore incorrect in stating that the date of the reference is December 1, 1998. December 1, 1998 is actually the date Accession AE001619 was submitted, not the date it was first seen (or publicly available).

The inventors had possession of the claimed invention before March 8, 1999, as evidenced by priority application US 60/114,060 filed December 28, 1998, specifically at Figures 1 and 2. Vaccine vectors and immunogenic compositions are described throughout US 60/114,060.

(b) Kalman's amino acid sequence differs from SEQ ID No:2

As traversed in the response filed September 11, 2003 and evidenced by the Examiner's own sequence comparison, Kalman's amino acid sequence is different from SEQ ID No:2 at least at two positions -- residues 282 and 291. Kalman's sequence is not the same as the sequence recited in the instant claims.

(c) Kalman does not disclose the vaccines and pharmaceutical compositions

As traversed in the response filed September 11, 2003, Kalman does not disclose the vaccines and pharmaceutical compositions because Kalman does not disclose or suggest expressing the sequences. In addition to the fact that Kalman's sequence is different from those recited in the instant claims, Kalman's sequences lack the structural feature of being operatively linked to one or more control sequences for expression of the polypeptide, as specified in some of the claims. Apart from the sequences being different, since Kalman's sequences are not in expressible form and are not capable of performing the intended use, Kalman et al does not anticipate the vaccines and compositions of the present application.

Withdrawal of the rejection of claims 44-62, 79, 86 and 87 under 35 U.S.C§102(a) is requested.

V. Rejection of the Claims Under 35 U.S.C. § 102(b) -- Commercial catalogs

The Examiner rejects claims 61 and 62 under 35 U.S.C.§102(b) as being anticipated by a number of commercial catalogs disclosing random primers, probes and linkers. Claims 61 and 62 are canceled, thereby rendering the rejection moot.

VI. Rejection of the Claims Under 35 U.S.C. § 102(a) -- WO 9927105 ('WO'105')

The Examiner rejects claims 44-62, 79, 86 and 87 under 35 U.S.C. §102(a) in view of WO'105. Applicants traverse this ground for rejection.

WO'105 was published on June 3, 1999. As stated above, the inventors had possession of the claimed invention before June 3, 1999, as evidenced by priority application US 60/114,060 filed December 28, 1998, specifically at Figures 1 and 2. Vaccine vectors and immunogenic compositions are described throughout US 60/114,060.

Withdrawal of the rejection of claims 44-62, 79, 86 and 87 under 35 U.S.C§102(a) is requested.

V. Rejection of the Claims Under 35 U.S.C. § 102(e) -- US patent 6,449,294 ('Griffais')

The Examiner rejects claims 44-62, 79, 86 and 87 under 35 U.S.C. 102(e) as being anticipated by Griffais. Applicants traverse this ground for rejection.

(a) Kalman's amino acid sequence differs from SEQ ID No:2

As traversed in the response filed September 11, 2003 and evidenced by the Examiner's own sequence comparison, Griffais' amino acid sequence is different from SEQ ID No:2 at least at two positions -- residues 282 and 291. Griffais' sequence is not the same as the sequence recited in the instant claims.

(b) Griffais' disclosure is not enabling for vaccines

Apart from the fact that Griffais' sequence is different from those recited in the instant claims, Applicants submit that Griffais does not provide an enabling disclosure that would anticipate claims 51-57, 59, 79, 83 and 88-93.

(i) What the instant application teaches

The presently amended claims are directed to vaccine vectors comprising a nucleic acid molecule encoding a specific protein (SEQ ID NO: 2) and to pharmaceutical compositions comprising such nucleic acid molecules.

As shown in Examples 1-3 in the specification, nucleic acid vaccines of the invention elicited a protective response against *C. pneumoniae* infection in mice. The specification provides complete details of how to make and use nucleic acid vaccines encoding SEQ ID NO: 2 and demonstrates that such vaccines are indeed useful.

(ii) What Griffais teaches

Griffais sequenced fragments of the *C. pneumoniae* genome and, with the assistance of computer implemented techniques, organized these fragments to create a map of the entire *C. pneumoniae* genome. By analyzing the *C. pneumoniae* genome to identify transcriptional start and stop codons in the *C. pneumoniae* genomic sequence, Griffais identified approximately 1300 putative open reading frames, which might encode proteins (see Table 1 of Griffais).

Using computer-implemented sequence homology analysis, Griffais compared these sequences to those found in sequence databases and, where possible, assigned putative functions to the open reading frames, based on their homology to known sequences.

The experimental work conducted by Griffais ends here.

As discussed in the instant specification, infection by *C. pneumoniae* is a major cause of community acquired pneumonia and perhaps also of other diseases.

There is accordingly great interest in a vaccine for the prevention of *C. pneumoniae* infection.

This is of course acknowledged by Griffais, and Griffais provides a generic discussion of how *C. pneumoniae* nucleic acid sequences might be used in the preparation of a vaccine. But while Griffais provides the sequence of the *C. pneumoniae* genome, he does not provide any helpful teaching as to how one might go about actually preparing a DNA vaccine.

(iii) Griffais' disclosure does not teach vaccines

Given the known principles of immunology, it is easy to speculate that one or more proteins expressed by *C. pneumoniae* might be candidates for potential use as a vaccine. This is just what Griffais does. Griffais merely postulates that any of the 1296 putative ORFs might work and then provides a discussion of typical approaches one might use to make a DNA-based vaccine. Griffais does not provide the critical guidance as to which if any of the putative open reading frames might provide a suitable vaccine candidate.

It is clear that Griffais contributes no more to the vaccine art than to offer up the entire genome of *C. pneumoniae*, comprising some 1.2 million nucleotides, and to identify some 1300 potential open reading frames and speculate as to the function of some of them.

(iv) In fact, Griffais' speculation is incorrect -- Only a few of the 1296 open reading frames can be used as vaccines

Applicants have determined that identifying a suitable *C. pneumoniae* sequence for use as a vaccine is no easy matter. Attached is a Declaration under 37 CFR § 1.132 of inventor Andrew Murdin, filed on US 10/334,137. The declaration states that, as part of the assignee's *C. pneumoniae* vaccine programme, 36 *C. pneumoniae* ORFs were tested in the *in vivo* mouse model described in Example 3. Only 8 of the 36 ORFs (i.e. 22%) provided a protective effect.

(v) Griffais' disclosure is not enabling for vaccines

Griffais' contribution is the sequence of the *C. pneumoniae* genome. Griffais does not provide vaccines nor useful teachings as to how to obtain them. Griffais offers no more than a generic description of standard vaccine methodology. Inviting the skilled artisan to search for a solution to the problem effectively by trial and error — in essence searching for the proverbial needle in a haystack — is not an enabling disclosure. A non-enabling reference does not anticipate (*In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). See also *Elan Pharmaceuticals v Mayo Foundation*. US Court of Appeals for the Federal Circuit, 00-1467, decided October 2, 2003:

> The issue is not whether the [prior art] teachings are an accurate compilation of the state of the scientific art at that time, [...] The issue is whether [the prior art] teachings enabled a person of ordinary skill, without undue experimentation, to produce the desired [result].

Based on the teachings of Griffais, considered as a whole (*W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)), the skilled person could not practice the instantly claimed invention without undue experimentation. Griffais therefore does not teach or suggest the instantly claimed subject matter. The insufficiency of the teachings of Griffais is made all the more clear by Applicants' own work showing that relatively few ORFs of *C. pneumoniae* are useful in the preparation of vaccines.

Withdrawal of the rejection under 35 U.S.C. §102(e) in view of Griffais is requested.

VI. Concluding Remarks

In view of the above amendments and remarks, reconsideration and favorable action on all pending claims are respectfully requested. If any questions or issues remain, the Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

If a fee is required for an extension of time which is not accounted for, such an extension is requested and the U.S.P.T.O. is authorized to withdraw from our Deposit Account Number 19-0741 any fee required.

Respectfully submitted,

Date: Feb 12, 2004

Michele M. Simkin
Registration No. 34,717

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5427
Facsimile: (202) 672-5399